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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/575,062 | DIOGUARDI, FRANCESCO SAVERIO | |
| | Examiner | Art Unit | |
| | Christina Marchetti Bradley | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-21 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/7/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Claims 1-21 and 32 are pending.

### *Priority*

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### *Claim Rejections - 35 USC § 112, second paragraph, and 101*

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-21 provide a process for the preparation of a composition comprising leucine and at least one of valine and isoleucine, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

5. Claims 1-21 are rejected under 35 U.S.C. 101 because the claimed recitation of a process, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### *Claim Rejections - 35 USC § 112, second paragraph*

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms and phrases "i.e.," and "etc." render the claims indefinite because it is unclear whether the limitations following the terms and phrases are part of the claimed invention. See MPEP § 2173.05(d). Claim 1 recites the term "i.e.". Claim 21 recites the term "etc."

8. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 3 and 4 recite the broad recitation 0.2 to 0.7, and the recitation 0.4 to 0.6 which is the narrower statement of the range/limitation. In the present instance, claim 6 recites the broad recitation 0.15 to 0.50, and the recitation 0.2 to 0.45 which is the narrower statement of the range/limitation. In the present instance, claim 7 recites the broad recitation 0.15 to 0.60, and the recitation 0.2 to 0.55 which is the narrower

statement of the range/limitation. In the present instance, claim 8 recites the broad recitation 10% to 50%, and the recitation 25% to 45% which is the narrower statement of the range/limitation. In the present instance, claim 11 recites the broad recitation 2% to 25%, and the recitation 5% to 15% which is the narrower statement of the range/limitation. In the present instance, claim 13 recites the broad recitation 10% to 505%, and the recitation 20% to 35% which is the narrower statement of the range/limitation. In the present instance, claim 14 recites the broad recitation at least 100%, and the recitation 150% to 350% which is the narrower statement of the range/limitation.

9. Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The phrase "molecular weight basis" in claims 3, 4, 6-8, 11, 13, 14, 16-20, and the phrase "the sum in gram molecular weight" in claim 15, is used by the claim to mean an amount, ratio or percentage. The accepted meaning of molecular weight is the sum of the weights of a molecule's constituent atoms. The accepted meaning of molecular weight does not pertain to a practical "weight" that can be used to create and use an amino acid composition as presently claimed. The phrase is indefinite because the specification does not clearly redefine the term.

***Claim Rejections - 35 USC § 112***

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1-21 and 32 are drawn to compositions comprising leucine and at least one of isoleucine and valine. The claims freely interchange the term "molecular weight" with the terms "amount," "ratio" and "percentage," in contradiction to the accepted meaning of the terms in the art. A molecular weight is the sum of the weights of a molecule's constituent atoms and not a practical "weight" that can be used to create and use an amino acid composition as presently claimed. In light of these facts, it is impossible practice the methods of the claims, specifically to prepare a composition with particular amounts of active ingredients when the amounts are expressed only in terms of molecular weight. As an example, it would be not possible to determine the molecular weight of a quantity of 1 gram of an amino acid because the molecular weight only refers to the molecule of the amino acid and not a unit of mass of that amino acid such a gram.

12. The specification contains no disclosure of how the amounts, ratios or percentages of the amino acids are to be measured and no units of measurement have been assigned to "molecular weight". In the pharmaceutical art, the only unit of measurement that is useful for expressing a dosage amount of drug in a given composition that is related to the molecular weight of the drug is in terms of the molar content of the drug. This can be in number of moles or a concentration of moles/unit of solvent, i.e., molar concentration. However, a mole and a molecular weight are not synonymous. As pointed out above, the molecular weight of a compound is merely the sum of the weights of a molecule's constituent atoms. A mole, on the other hand, is the amount of a substance with a weight in grams numerically equal to the molecular weight of the substance. So, for instance, if 1 mole of the amino acid arginine were identified, then the amount in grams of

arginine would be 1 times the molecular weight of arginine expressed in grams, i.e., 1 x 174.20 or 174.20 g. Alternatively, in the pharmaceutical arts, amounts and ratios of ingredients can be designated in units of mass such as grams or percent mass relative to the total mass or volume of the composition.

13. The instant specification uses the term "gram-moles" and "gram molecular weights" to describe the compositions. At page 4, line 26 to page 5, line 10, it is set forth:

> " … the studies underlying the present invention have enabled identification of a stoichiometric mixture of amino acids that would enable maximum use for synthetic purposes, optimizing, at the same time, coverage of the energy requirement of the mitochondrial energy metabolism. According to the invention:
> 1) the mixture envisages the use of the branched amino acid leucine in combination with at least one between, and preferably both of, the branched amino acids isoleucine and valine. The ratios, expressed in **gram-moles** between the amino acids, in proportion to 1 gram-mole of L-Leucine, can be identified as follows:
> L-Isoleucine: from 0.2 to 0.7, preferably from 0.4 to 0.6;
> L-Valine: from 0.2 to 0.7, preferably from 0.4 to 0.6.
> 2) The mixture envisages, as further active ingredients, at least one between, and possibly both of, the amino acids threonine and lysine. The ratios, expressed in **gram-moles** between the amino acids, in proportion to 1 gram-mole of L-Leucine, can be identified as follows:
> L-Threonine: from 0.15 to 0.50, preferably from 0.2 to 0.45;
> L-Lysine: from 0.15 to 0.60, preferably from 0.3 to 0.55.
> At the current state of the studies conducted by the inventor, the formulation that appears to present a greater degree of activity is a formulation in which, setting at 1 the sum of leucine, isoleucine and valine, in the reciprocal dimensions based upon the **gram molecular weight** identified in point 1), the sum of threonine and lysine is between 10% and 50% of said formulation (always on the basis of the **gram molecular weight** of the substances in question), and preferably between 25% and 45%.
> 3) The nutritional intake of the mixture can be integrated with one or more further essential amino acids, and in particular histidine, methionine, phenylalanine, tryptophan. Setting at 1 the sum of leucine, isoleucine, valine, threonine and lysine, the other essential amino acids (histidine, methionine, phenylalanine, tryptophan) are represented in a global amount (again expressed as **gram molecular weight/gram molecular weight ratios**) ranging from 2% to 25%, and preferably from 5% to 15%. " **emphasis added**

The terms "gram-moles" and "gram molecular weights" are not defined in the specification and

are not typically used in the pharmaceutical arts to express amounts of substances. Furthermore, molecular weights do not have a unit of "value" except the sum total of the weight of atoms which constitute a given molecule. While a term used in the claims may be given a special meaning in the description of the invention, no term may be given a meaning repugnant to the usual meaning of the term.

14. For these reasons and for the reasons presented below, claims 1-21 and 32 are rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement.

15. Claims 1-21 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention. To comply with the enablement requirements of 35 U.S.C. §112, first paragraph, a specification must adequately teach how to make and how to use a claimed invention throughout its scope, without undue experimentation. *Plant Genetic Systems N.V. v. DeKalb Genetics Corp.*, 315 F.3d 1335, 1339, 65 USPQ2d 1452, 1455 (Fed. Cir. 2003). There are a variety of factors which may be considered in determining whether a disclosure would require undue experimentation. These factors include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

*Nature of the invention.*

Claims 1-21 are directed to processes of preparing compositions comprising a combination of known amino acids. It is disclosed that these compositions may be used for such purposes as maintaining intact and/or restoring and/or increasing the number of cellular mitochondria, for modifying in a positive sense the activity of production of intracellular energy, and treating pathological conditions characterized by insufficient or reduced mitochondrial function. Claim 32 is directed to a method for treating pathological conditions characterized by insufficient or reduced mitochondrial function by administering compositions of leucine and at least one of valine or isoleucine.

*State of the prior art*

Amino acid compositions containing combinations of amino acids as claimed were well known in the prior art. For example, Dudrick et al. (U.S. Patent No. 5,026,721) discloses amino acid compositions for nutritional supplementation for enhancing physical performance (see the abstract) and Bergstr6m et al. (U.S. Patent No. 3,764,703) who teach amino acid compositions intended to provide nitrogen nutrition for patients suffering from uremic conditions (see the abstract). These references, which are representative of the prior art concerning amino acid compositions, use meaningful units of measure in teaching the amounts of amino acids to be contained in their compositions. Bergstr6m et al. teach molar quantities at col. 2, lines 23-46 as well as grams of amino acid/liter of amino acid composition at col. 4, Example 5. Dudrick et al. teach the specific distribution of amino acids based on the weight percentage of each amino acid based on the total weight in grams of the amino acids in the mixture (see for example, col. 4, Tables 1-2 and col. 6, example 6).

The compositions of the instant invention are intended for the use of treating conditions related to insufficient mitochondrial function. The prior art recognizes over 80 disorders that are associated with disturbances of mitochondrial function (see Table 2 of Naviaux RK. The Spectrum of Mitochondrial Disease, in Mitochondrial and Metabolic Disorders: A Primary Care Physician's Guide, 2nd ed. 2003). The conditions include those involving the regulation of fuel homeostasis such as Leigh syndrome, those associated with mtDNA mutations, such as Pearson Marrow syndrome, and those associated with intramitochondrial enzymes, such as Maple syrup urine disease, as well as disorders sometimes associated with mitochondrial dysfunction such as aging and multiple sclerosis. Naviaux writes: "No single drug, diet or vitamin has emerged as a panacea for mitochondrial disease. Time and again, physicians working at specialized metabolic centers are reminded that every child is biochemically unique. Two children with precisely the same point mutation their DNA, nominally leading to the same disease, may respond to medication and nutritional interventions in different ways...Because mitochondrial and metabolic disorders involve defects at an exceedingly fundamental level in cell function, no vitamin or cofactor therapy is curative except in very rare and specific disorders." (p. 9) Thus, pathological conditions characterized by insufficient or reduced mitochondrial function include a broad spectrum of diseases and that cannot be uniformly treated.

*Level of ordinary skill in the art.*

The level of ordinary skill in the amino acid supplement art is high. However, given the state of the art as set forth above where conventional units of measure are used to determine the amounts/proportions of amino acids to be used in amino acid compositions, the artisan would not be able to determine the amino acids amounts/proportions given the present disclosure because

applicant's disclosure is based upon a "molecular weight" basis of amounts/proportions which was not recognized in the art as being a meaning manner in which to determine amino acid amounts/proportions in amino acid composition of the type claimed.

The level of ordinary skill in the mitochondrial disease art is low. As Naviaux points out, there is no single effective treatment that covers the broad spectrum of mitochondrial diseases.

*Level of predictability in the art*

The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. See MPEP 2164.03. Here, while the art was well aware of amino acid compositions of the type claimed and uses therefore, the art was not aware of the how to make amino acid compositions based solely on a basis of molecular weights of the amino acids that constitute the composition. Conventional units of measure, such as those discussed above, would be necessary to make amino acids compositions. Lacking such units of measure, it could not be predicted how to make the presently disclosed and claimed amino acid compositions.

The level of predictability in the mitochondrial disease art is low. As Naviaux points out, there is no single effective treatment that covers the broad spectrum of mitochondrial diseases. In addition, Naviaux warns that "over-the-counter health food supplements are considered food products rather than medicine; their quality is not regulated by the FDA, nor is there any published, peer-reviewed research that has tested the efficacy of these supplements in patients with mitochondrial disease." (p. 9). Platell *et al.* (*J. Gastroenterology and Hepatology*, **2000**, *15*,

706-17, abstract) specifically address the use of compositions comprising the branched-chain amino acids (BCAA) leucine, valine and isoleucine. Platell *et al.* state: "By far the most intensively studied applications for BCAA have been in patients with liver failure and/or patients in catabolic disease states. However, the resulting studies have not demonstrated a clear clinical benefit for BCAA nutritional supplements. In patients with liver failure, the BCAA did improve nitrogen retention and protein synthesis, but their effect on patient outcome was less clear. Similarly, in critically ill septic patients, BCAA did not improve either survival or morbidity. The BCAA are important nutrients, and it seems that nay specific benefits associated with their use will be bases upon a greater understanding of the underlying cellular biology." Thus, the effect of compositions comprising BCAA on patients suffering from mitochondrial diseases is not predictable even when the compositions positively affect some aspects of the disease state.

*Amount of direction and guidance provided by the inventor.*

The guidance given by the specification is to make the amino acid compositions based on the molecular weights of the individual amino acids or ratios of amino acid molecular weights. This direction and guidance, however, would not satisfy the requirements of 35 U.S.C. 112, first paragraph because, as explained above, it does not convey to the skilled artisan in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the disclosed amino acid compositions.

The specification provides little guidance as to the specific conditions that can be treated with the claimed compositions. Given the breadth of conditions recognized in the art to be associated with mitochondrial dysfunction and the unpredictability in the art, such guidance is

critical for the skilled artisan to practice the invention.

*Existence of working examples.*

At pages 6-14 of the present specification, it is reported that elderly subjects were administered amino acid compositions according to the invention. Resulting effect on mitochondrial activity are shown. However, the specific amino acid composition, in terms of actual amounts/proportions, is not identified. In addition, the specific condition of the patient population or the mitochondrial dysfunction-related pathological state was not defined.

*Breadth of claims.*

The claims are directed to the preparation of specific amino acid compositions and to methods of treatment in which such compositions are administered. The genus of conditions characterized by insufficient mitochondrial function is exceptionally broad and includes those involving the regulation of fuel homeostasis such as Leigh syndrome, those associated with mtDNA mutations, such as Pearson Marrow syndrome, and those associated with intramitochondrial enzymes, such as Maple syrup urine disease, as well as disorders sometimes associated with mitochondrial dysfunction such as aging and multiple sclerosis.

*Quantity of experimentation*

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with these claims. Applicant has failed to provide guidance and information to allow the skilled artisan to ascertain how to make, and thus how to use an amino acid composition to accomplish the stated objectives because molecular weights have been incorrectly equated to amounts. The skilled artisan would not be able to use

molecular weights, in and of themselves, to determine how much of the amino acids to employ to produce an amino acid composition or to accomplish the disclosed objectives.

***Search***

16. As noted above, this application it includes terminology which is so different from that which is generally accepted in the art to which this invention pertains that a proper search of the prior art cannot be made. Specifically, it is not possible to search the limitations in claims 3, 4, 6-8, 11 and 13-20 pertaining to molecular weight. In addition, claims 1-21 fail to recite active method steps. Therefore, only a limited search of the compositions recited in claims 1, 2, 5, 9, 10, 12 and 21 was conducted. Claim 32 was fully searched.

Applicant is required to provide a clarification of these matters or correlation with art-accepted terminology so that a proper comparison with the prior art can be made. Applicant should be careful not to introduce any new matter into the disclosure (i.e., matter which is not supported by the disclosure as originally filed).

***Claim Rejections - 35 USC § 102***

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1, 2, 5, 9, 10, 12 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Ozeki *et al.* (U.S. Patent No. 5,036,052). Ozeki *et al.* teach a method of preparing a composition comprising the amino acids leucine, isoleucine, valine, threonine, lysine, histidine, methionine, phenylalanine, and tyrosine (Table 1). With respect to claim 21, the pH of the

composition is 6.5 (Example 1). Ozeki *et al.* also teach a method of preparing a composition comprising leucine, isoleucine, valine, threonine, lysine, histidine, methionine, phenylalanine, tryptophan, tyrosine and cysteine (Table 45). Ozeki *et al.* do not teach that the resulting compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions are identical to the compositions prepared in the claimed method, the prior art of Ozeki *et al.* inherently meets these functional limitations.

19. Claims 1, 2, 5 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Germano (U.S. Patent No. 6,503,506). Germano teaches a method for making a nutritional supplement for treating chronic debilitating diseases to overcome conditions of oxidative stress, decreased lean muscle mass and decreased energy production (mitochondrial failure), the supplement comprising the amino acids leucine, isoleucine, valine and lysine (abstract, col. 8, ln. 45 to col. 9, ln. 10). Germano teaches a method of treating in which the patient takes two one-bottle servings of the supplement (col. 8, ln. 49).

20. Claims 1, 2, 5, 9, 10, 12 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Dioguardi (U.S. Patent No. 6,218,420). Dioguardi teaches a method of preparing a composition comprising the amino acids leucine, isoleucine, valine, threonine, lysine, cysteine, histidine, methionine, phenylalanine, and trypotphan (Table 1). With respect to claim 21, the pH of the composition is in the physiological range (claim 2). Dioguardi does not teach that the resulting compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions are identical to the

compositions prepared in the claimed method, the prior art of Dioguardi inherently meets these functional limitations.

21. Claims 1, 2, 5, 9, 10 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Conti *et al.* (U.S. 20040192756). Conti *et al.* teach a method of preparing a composition comprising the amino acids leucine, isoleucine, valine, threonine, lysine, cysteine, histidine, methionine, phenylalanine, tyrosine and trypotphan (paragraph 0022). Conti *et al.* do not teach that the resulting compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions are identical to the compositions prepared in the claimed method, the prior art of Conti *et al.* inherently meets these functional limitations.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

22. Claims 1, 2, 5, 9, 10 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Conti *et al.* (U.S. 20040157903). Conti *et al.* teach a method of preparing a composition comprising the amino acids leucine, isoleucine, valine, threonine, lysine, methionine, phenylalanine, histidine, trypotphan, cysteine and tyrosine (paragraph 0018). Conti *et al.* do not teach that the resulting compositions can be used to maintain intact and/or restore and/or increase

the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions are identical to the compositions prepared in the claimed method, the prior art of Conti *et al.* inherently meets these functional limitations.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

***Double Patenting***

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 1, 2, 5, 9, 10, 12 and 21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,218,420. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-9 of U.S. Patent No. 6,218,420 recite a composition comprising up to 75% leucine, isoleucine and valine, up to 50% threonine and lysine, and up to 40% of cysteine, histidine, phenylalanine, methionine, tryptophan and tyrosine. Claims 1-9 of U.S. Patent No. 6,218,420 do not recite a method of preparing the compositions. It would have been obvious to prepare the compositions comprising up to 75% leucine, isoleucine and valine, up to 50% threonine and lysine, and up to 40% of cysteine, histidine, phenylalanine, methionine, tryptophan and tyrosine, satisfying the limitations of instant claims 1, 2, 5, 9, 10, 12 and 21. The skilled artisan would have been motivated to do so in light of claims 8 and 9 of U.S. Patent No. 6,218,420 which state that the compositions can be used to regulate nitrogen in a body. Claims 1-9 of U.S. Patent No. 6,218,420 do not state that the compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions recited in claims 1-9 of U.S. Patent No. 6,218,420 are identical to the compositions prepared in the instantly claimed methods, the compositions of claims 1-9 of U.S. Patent No. 6,218,420 inherently meet these additional functional limitations.

25. Claims 1, 2, 5, 9, 10, 12 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 16-35 of copending application 12/104,722. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 16 of copending application 12/104,722 recites a composition

comprising leucine, isoleucine and valine. Claim 17 recites a composition further comprising threonine and lysine. Claim 19 recites a composition further comprising methionine, phenylalanine, histidine and trypotphan. Claim 22 recites a composition further comprising tyrosine and cysteine. Claims 16-35 of copending application 12/104,722 do not recite a method of preparing the compositions. It would have been obvious to prepare the compositions recited 16-35 of copending application 12/104,722, satisfying the limitations of instant claims 1, 2, 5, 9, 10, 12 and 21. The skilled artisan would have been motivated to do so because claim 16 of copending application 12/104,722 states that the compositions can be used to improve ventricular function in a patient suffering from diabetes. Claims 16-35 of copending application 12/104,722 do not state that the compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions recited in claims 16-35 of copending application 12/104,722 are identical to the compositions prepared in the instantly claimed methods, the compositions of claims 16-35 of copending application 12/104,722 inherently meet these additional functional limitations. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

26. Claims 1, 2, 5, 9, 10, 12 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-54 of copending application 10/486,141. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 23 of copending application 10/486,141 recites a composition comprising leucine, isoleucine, valine, lysine, and threonine, and at least one of alanine,

methionine, histidine and tryptophan. Claim 26 recites a composition further comprising methionine and tyrosine. Claim 27 recites a composition further comprising cysteine. Claims 23-54 of copending application 10/486,141 do not recite a method of preparing the compositions. It would have been obvious to prepare the compositions recited 23-54 of copending application 10/486,141, satisfying the limitations of instant claims 1, 2, 5, 9, 10, 12 and 21. The skilled artisan would have been motivated to do so because claim 23 of copending application 10/486,141 states that the compositions can be used to heal or mend corneal lesions. Claims 23-54 of copending application 10/486,141 do not state that the compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions recited in claims 23-54 of copending application 10/486,141 are identical to the compositions prepared in the instantly claimed methods, the compositions of claims 23-54 of copending application 10/486,141 inherently meet these additional functional limitations. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

27. Claims 1, 2, 5, 9, 10, 12 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 10 and 12-29 of copending application 10/480,774. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 9 of copending application 10/480,774 recites a composition comprising leucine, isoleucine and valine. Claim 10 recites a composition further comprising threonine and lysine. Claim 12 recites a composition further comprising cysteine, methionine, phenylalanine, tyrosine and tryptophan. Claim 14 recites a composition further

comprising phenylalanine. Claims 9, 10 and 12-29 of copending application 10/480,774 do not recite a method of preparing the compositions. It would have been obvious to prepare the compositions recited 9, 10 and 12-29 of copending application 10/480,774, satisfying the limitations of instant claims 1, 2, 5, 9, 10, 12 and 21. The skilled artisan would have been motivated to do so because claim 16 of copending application 10/480,774 states that the compositions can be used to improve myocardial ventricular function in patients suffering from type II diabetes. Claims 9, 10 and 12-29 of copending application 10/480,774 do not state that the compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions recited in claims 9, 10 and 12-29 of copending application 10/480,774 are identical to the compositions prepared in the instantly claimed methods, the compositions of claims 9, 10 and 12-29 of copending application 10/480,774 inherently meet these additional functional limitations. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

28. Claims 1, 2, 5, 9, 10, 12 and 21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 33-54 of copending application 10/332,236. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claim 33 of copending application 10/332,236 recites a composition comprising leucine, isoleucine and valine. Claim 34 recites a composition further comprising threonine. Claim 34 recites a composition further comprising one or more of cysteine, methionine, phenylalanine, histidine, tyrosine and tryptophan. Claim 36 recites a composition

further comprising lysine. Claims 33-54 of copending application 10/332,236 do not recite a method of preparing the compositions. It would have been obvious to prepare the compositions recited 33-54 of copending application 10/332,236, satisfying the limitations of instant claims 1, 2, 5, 9, 10, 12 and 21. The skilled artisan would have been motivated to do so because claim 33 of copending application 10/332,236 states that the compositions can be used to treat chronic heart failure. Claims 33-54 of copending application 10/332,236 do not state that the compositions can be used to maintain intact and/or restore and/or increase the number of cellular mitochondria or to modify the production of intracellular energy. Because the chemical structure and physical composition of the compositions recited in claims 33-54 of copending application 10/332,236 are identical to the compositions prepared in the instantly claimed methods, the compositions of claims 933-54 of copending application 10/332,236 inherently meet these additional functional limitations. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Conclusion***

29. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Marchetti Bradley whose telephone number is (571)272-9044. The examiner can normally be reached on Monday-Thursday, 9:00 A.M. to 3:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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